GlaxoWellcome

March 29, 1999

Management Dockets
Dockets Management Branch (HFA-305) 99 MAR 31 A9:48
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20857

Re: Docket Number: 98D-1267

Dear Sirs:

Please find enclosed GlaxoWellcome's comments on the draft Guidance for Industry-NDAs: Impurities in Drug Substances.

Please feel free to call me at (919) 483-6408 if you need additional information or clarification regarding the comments.

Sincerely,

Suva B. Roy

Suva B. Roy, Ph. D.
Director, Chemistry Pharmacy and Manufacturing
Regulatory Affairs and Quality Division

98D-1267

C1

Glaxo Wellcome Inc.
Five Moore Drive
PO Box 13398
Research Triangle Park
North Carolina 27709-3398

Telephone
919 483 2100

Comments from GlaxoWellcome on the Draft Guidance for Industry
NDAs: Impurities in Drug Substances

General Comments

The guidance proposes to apply ICHQ3A requirements to already approved drug substances (DS). These drugs have already been proven to be safe and effective with the currently approved specifications. Applying ICHQ3A requirements would not enhance the safety or the efficacy of these drugs. This guidance does not add value. We highly recommend that the guidance be dropped. Alternatively, we recommend that the rationale for the guidance be clearly enunciated in the preamble to the document.

Specific Comments

This draft guidance states that changes in DS synthesis or process requiring supplements will trigger the compliance to the ICHQ3A guidance. The BACPAC-I and BACPAC-II will change the submission requirements for DS changes. We recommend that:

1) This document cross-references the BACPAC-I and BACPAC-II guidances.
2) Only supplements for prior approval trigger the provisions of this guidance.
3) The Agency holds off on finalizing this guidance until both BACPAC-I and BACPAC-II are final. This will allow for a more comprehensive and systematic implementation of the new regulatory requirements for drug substances.

The draft guidance is also silent on the qualification requirements for impurities and degradation products that exceed the ICHQ3A thresholds. We strongly recommend that the guidance clearly state that preclinical safety studies will not be required since these impurities and degradation products are already approved at these levels and have been proven in human use.